REMARKS

Applicants have amended their claims in order to further clarify the definition of the present invention, so as to simplify and limit issues remaining in the application. Specifically, Applicants have amended claim 1 to delete various of the parenthetical items; to recite that the compound (I) "is" obtained by reacting a specified compound (II) with a sugar (III); to recite that the compound (II) is selected from the group B consisting of doxorubicin and a peptide; and to further define the sugar (III) of group A, this group A consisting of lactose, sialyllactose, and a compound prepared by chemically binding a polymer selected from the group consisting of polyoxyethylene, polygutamic acid and polyvinylpyrrolidone to a hydroxyl group other than the hydroxyl group formed from the reducing aldehyde group of a sugar selected from the group C, with this group C consisting of lactose and sialyllactose. Claim 2 has been amended to recite that the compound (II) is a pharmaceutical compound, and claim 3 has been amended to recite that the compound (II) is a peptide. The parenthetical expression for claim dependency in claim 4 has been amended. Claims 5, 9, 13, 17 and 23 have been amended to recite respective preparations obtained by specified processing steps; and claim 21 has been amended to recite that the compound (II) is enkephalin. For simplifying issues and facilitating proceedings, claims 6-8, 10-12, 14-16, 18-20, 22 and 24-60 have been cancelled without prejudice or disclaimer.

In addition, Applicants are adding new claims 61-80 to the application. Claim 61, dependent on claim 1, recites that the preparation is obtained by specified steps including encapsulating the compound (II) and the sugar (III) in a pharmaceutical

carrier, with the compound (II) and the sugar (III) being reacted to give to the compounds (I) in the carrier; and claim 62, dependent on claim 5 or 61, defines specific materials for the pharmaceutical carrier. Claim 63, dependent on claim 2, recites that the preparation is obtained by specified steps including encapsulating the pharmaceutical compound and the sugar (III) in a pharmaceutical carrier, with the pharmaceutical compound being reacted with the sugar (III) to give the compound (I) in the pharmaceutical carrier; and claim 64, dependent on claim 9 or 63, defines specific materials for the pharmaceutical carrier. Claims 65, 67 and 69, dependent respectively on claims 3, 4 and 21, define the preparation in terms of how the preparation is made; and claims 66, 68 and 70, dependent respectively on claims 13 or 65, 17 or 67 and 23 or 69, define material of the pharmaceutical carrier. Similarly, claims 71, 73, 75, 77 and 79, dependent respectively on claims 1, 2, 3, 4 and 21, define the preparation in terms of processing steps for forming the preparation; and claims 72, 74, 76, 78 and 80, dependent respectively on claims 71, 73, 75, 77 and 79, define materials for the pharmaceutical carrier.

Initially, it is respectfully requested that the present amendments be entered. Noting, in particular, the bases for rejection of claims under 35 USC §112, and as will be discussed in detail infra, it is respectfully submitted that the present amendments clearly materially limit issues remaining in connection with the above-identified application, and at the very least present the claims in better form for appeal. Moreover, it is respectfully submitted that the present amendments, further defining various features of the present invention as previously set forth in the claims, do not raise any new issues, including any issue of new matter. Noting

clarifications by the Examiner in the Office Action mailed April 1, 2004, it is respectfully submitted that the present amendments are timely.

Moreover, while new claims 61-80 are being added to the application, note that a greater number of claims than the number of claims being added are being cancelled in the present Amendment; accordingly, after entry of the present amendments, the number of claims remaining in the application will be less than the number of finally rejected claims.

In view of all of the foregoing, it is respectfully submitted that Applicants have made the necessary showing under 37 CFR § 1.116(c); and that, accordingly, entry of the present amendments is clearly proper.

Applicants respectfully traverse the rejection of their claims under the first paragraph of 35 USC §112, as set forth in Item 5 on page 2 of the Office Action mailed April 1, 2004, particularly insofar as this rejection is applicable to the claims as presently amended. Thus, claim 1 has been amended to recite that the compound (II) having a free amino group is selected from the group B, with B consisting of doxorubicin and a peptide; and that the sugar (III) is selected from the group A, the group A consisting of lactose, sialyllactose and compounds prepared by chemically binding a polymer selected from the group consisting of polyoxyethylene, polyglutamic acid and polyvinylpyrrolidone to a hydroxyl group other than the hydroxyl group formed from the reducing aldehyde group of a sugar selected from the group C, wherein the group C consists of lactose and sialyllactose. Thus, in view of the further definition of groups A, B and C in presently amended claim 1, it is respectfully submitted that the basis for the rejection of the claims under the first

paragraph of 35 USC §112 is moot. Specifically, the present claims do not recite "all the compounds having a free amino group", the present claims reciting specific compounds, such that contentions by the Examiner with respect to the claims covering "all the compounds having a free amino group" are moot.

Applicants respectfully traverse the rejection of claims under the second paragraph of 35 USC §112, as being indefinite, set forth in Item 6 on pages 2-4 of the Office Action mailed April 1, 2004, particularly insofar as this rejection is applicable to the claims as presently amended. Thus, various of the letters in parentheses have been deleted; it is respectfully submitted that the remaining parentheses are used for clearly distinguishing the following three compounds, namely, Compound (II): a compound having a free amino group selected from the group B; Compound (III): a sugar having the reducing power selected from the group A; and Compound (I): a reaction product of Compound (II) and Compound (III). It is respectfully submitted that the remaining uses of parentheses in the claims clarify the meaning of claims by providing a short hand expression for the various compounds, and further clarify the claims.

Applicants have deleted the term "derivative" from claim 3, so that this basis for the indefiniteness rejection is moot.

Applicants respectfully traverse the contention by the Examiner that the phrase "modified with or encapsulated in" renders claims confusing. As will be shown in the following, it is respectfully submitted that, illustratively (and not to be limiting), the specification of the above-identified application discloses four embodiments as methods of preparing the claimed preparation. In view of these

four embodiments, it is respectfully submitted that the phrase "modified with or encapsulated in" is sufficiently clear such that one of ordinary skill would know whether any specific preparation fell within or outside the scope of the present claims. It is respectfully submitted that, under the present circumstances, the second paragraph of 35 USC §112 requires nothing more. See In re Moore, 169 USPQ 236 (CCPA 1971).

In the following will be provided a discussion of these four embodiments in Applicants' original disclosure; this discussion refers to the enclosed prepared figures.

Thus, an Embodiment (1) is an embodiment wherein a compound (II) having a free amino group is modified with a pharmaceutical carrier. In this embodiment, a free amino group of the modified compound (II) is reacted with an aldehyde group of a sugar (III) having the reducing power, outside of the pharmaceutical carrier.

An Embodiment (2) includes three subtypes, namely, (2a), (2b) and (2c). In subtype (2a), a compound (II) having a free amino group and a sugar (III) having the specified reducing power are simultaneously encapsulated in the pharmaceutical carrier. In subtype (2b), the sugar (III) having the reducing power is encapsulated in the pharmaceutical carrier after a compound (II) having a free amino group is encapsulated therein. In subtype (2c), a compound (II) having a free amino group is encapsulated in the pharmaceutical carrier after a sugar (III) having the reducing power is encapsulated therein. In each of these subtypes of Embodiment (2), a compound (II) having a free amino group and a sugar (III) having the reducing power are encapsulated in a pharmaceutical carrier. In these subtypes of Embodiment (2),

a free amino group of the compound (II) is reacted with an aldehyde group of the sugar (III) having the reducing power to give a compound (I) in the pharmaceutical carrier.

An Embodiment (3) is an embodiment wherein a compound (I) is obtained by reacting a compound (II) having a free amino group and a sugar (III) having the reducing power outside of a pharmaceutical carrier, and a part of a compound (II) moiety in the compound (I) is modified with a pharmaceutical carrier.

An Embodiment (4) is an embodiment wherein a compound (I) is obtained by reacting a compound (2) having a free amino group and a sugar (III) having the reducing power outside of a pharmaceutical carrier, and the whole compound (I) is encapsulated in the pharmaceutical carrier.

These various embodiments are shown in the enclosed figures, showing exemplary illustrations of Embodiments (1), (2) (a)-(c), (3) and (4). It is respectfully submitted that Applicants' disclosure as a whole shows what is meant by modified with or encapsulated with, such that these terms are not confusing as set forth in the claims.

The question by the Examiner as to what the term "modified with or encapsulated in" defines, set forth on page 3 of the Office Action mailed April 1, 2004, is noted. It is respectfully submitted that the foregoing clearly shows what is meant by the term "modified with or encapsulated in", such that the term is not confusing to one of ordinary skill in the art.

The word "included" has been deleted from claim 5, avoiding this basis for the indefiniteness rejection.

Claims 5, 9, 13, 17 and 23 have been amended to delete the expression "which can be obtained", thereby rendering moot this basis for rejection of the claims as indefinite.

The rejection of claims as being vague and unclear "because it is not clear what is being encapsulated in a pharmaceutical carrier", is respectfully traversed. As seen previously herein, and is clear from Applicants' disclosure, the compound having a free amino group and a sugar having the reducing power are incorporated in a pharmaceutical carrier (e.g., Embodiment (2) in the foregoing); or the resultant compound from the reaction of a compound having a free amino group with a sugar having the reducing power is encapsulated in a pharmaceutical carrier (see Embodiment (4) as discussed previously). It is respectfully submitted that the claims, particularly as presently amended, are clear as to what is being encapsulated in the pharmaceutical carrier.

Rejection of claim 8 as being indefinite, because of the term "included", is moot, various of the claims reciting "encapsulation".

Comments by the Examiner in Item 7 on page 4 of the Office Action mailed April 1, 2004, are noted. It is respectfully submitted that the language "can be obtained" has been deleted from the claims as presently amended.

The additional contention by the Examiner that the labeling of compounds "does not clarify as to what is being released", the compound with free amino group, the sugar having the reducing power or the product of the reaction between the compound with free amino group and the sugar having the reducing power, is noted. Note that claim 1 recites that the compound (I) can rapidly release the compound (II)

having a free amino group in response to changes in pH; it is respectfully submitted that the claims are clear as to what is being released. Moreover, the compounds (II) and (III) are defined with respect to specific materials for the Groups A, B and C; it is respectfully submitted that this is sufficient to satisfy the requirements of 35 USC §112, second paragraph, with respect to the metes and bounds of the present invention. See In re Moore, supra.

Applicants respectfully submit that all of the claims presented for consideration by the Examiner patentably distinguish over the teachings of the references applied by the Examiner in rejecting claims in the Office Action mailed April 1, 2004, that is, the teachings of U.S. Patent No. 5,580,543 to Sessler, et al., Japanese Patent Document No. 07-61999 (Katsukiyo), and Japanese Patent Document No. 09-263579 (Masashi, et al.), under the provisions of 35 USC §102 and 35 USC §103.

It is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such a pharmaceutical preparation as in the present claims, including the compound (I) obtained by reacting a compound (II) having a free amino group with a sugar (III) having the reducing power, wherein the compound (II) having the free amino group is selected from the group consisting of doxorubicin and a peptide, and the sugar (III) having the reducing power is selected from the group consisting of lactose and sialyllactose, and compounds prepared by chemically binding a polymer selected from the group consisting of polyoxyethylene, polyglutamic acid and polyvinylpyrrolidone to a hydroxyl group other than the hydroxyl formed from the reducing aldehyde group of

a sugar selected from the Group C, wherein the Group C consists of lactose and sialyllactose. See claim 1.

In addition, it is respectfully submitted that these references would have neither taught nor would have suggested the other aspects of the present invention as in the remaining, dependent claims, including wherein the preparation is obtained by the steps as set forth in claims 5, 9, 13, 17, 23, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79; and/or materials of the pharmaceutical carrier as in claims 62, 64, 66, 68, 70, 72, 74, 76, 78 and 80; and/or wherein the compound (II) is a pharmaceutical compound (see claim 2), or a peptide (see claim 3), particularly wherein this peptide is insulin (see claim 4), or wherein this compound (II) is an enkephalin (see claim 21).

According to the present invention, a pharmaceutical preparation, which is pH responsive and which is capable of rapidly releasing a compound having a free amino group such as an amino acid derivative, a peptide, a protein or an enzyme, can easily be prepared and used. The pharmaceutical preparation is capable of releasing various compounds having a free amino group in response to changes in pH, and releases such compounds specifically at target parts at which the pH is lowered due to the occurrence of inflammation, tumor or the like to cause the compounds to exhibit better effects. Since the pharmaceutical preparation releases the various compounds at only target points, a reduction of side effects can be achieved.

These advantages are achieved according to the present invention, which is obtained by reacting specified compounds; that is, e.g., a compound (II) having a

free amino group and selected from the group consisting of doxorubicin and a peptide, with a sugar (III) having reducing power and selected from the group A, as in the present claims.

Sessler discloses use of texaphyrins for radiation sensitization, the texaphyrins enhancing radiation damage and overcoming many of the drawbacks of prior art radiation sensitizers. See column 3, lines 51-54. As to what is meant by a texaphyrin, note lines 3 and 4 of column 4. See also column 6, lines 19-22 and 30-40; and column 7, lines 14-30. Note also column 10, lines 55-58, disclosing pharmaceutical preparations which may be administered alone or in combination with pharmaceutically acceptable carriers, in either single or multiple doses. Note also column 13, lines 8-14 of this patent.

It is emphasized that Sessler, et al. is directed to inclusion of texaphyrins as radiation sensitizers. It is respectfully submitted that this reference does not disclose, nor would have suggested, pharmaceutical preparations including the compound (I) obtained by reacting a compound (II) selected from the group consisting of doxorubicin and a peptide with a sugar (III), inter alia, selected from the group A (consisting of lactose and sialyllactose, and compounds prepared by chemically binding a polymer selected from a specified group to a hydroxyl group other than the hydroxyl group formed from the reducing aldehyde group of a sugar selected from the group consisting of lactose and sialyllactose), as in the present claims, and advantages thereof.

It is respectfully submitted that the additional teachings of the two applied Japanese patent documents would not have rectified the deficiencies of Sessler, et

al., such that the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art.

Katsukiyo discloses a saccharide-modified protein which has increased ability to accumulate in the liver and increased physiological activity. The protein is achieved by reacting a lactose-lactone with a protein in an aqueous medium at 0-45°C, with the protein being characterized by being a bound reaction product from lactose-lactone and a protein (except interferon-alpha).

Masashi discloses a compound derivative consisting of a specific piperidine derivative having amide groups and useful as a constituent component of a drug carrier, the piperidine derivative being expressed by the formula I as described in this patent document.

Even assuming, arguendo, that the teachings of the two Japanese patent documents were properly combinable with the teachings of Sessler, et al., such combined teachings would have neither disclosed nor would have suggested the presently claimed preparation, including the compounds (II) and (III) reacted with each other to form the compound (I) of the preparation.

In view of the foregoing comments and amendments, entry of the present amendments, and reconsideration and allowance of all claims remaining in the application, are respectfully requested.

To the extent necessary, Applicants petition for an extension of time under 37 CFR 1.136. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to the Antonelli, Terry, Stout & Kraus,

LLP Deposit Account No. 01-2135 (Docket No. 506.40278X00), and please credit any excess fees to such Deposit Account.

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP

By _____
William I. Solomon
Reg. No. 28,565

1300 North Seventeenth Street
Suite 1800
Arlington, Virginia 22209
Telephone: (703) 312-6600
Facsimile: (703) 312-6666
WIS/sjg